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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/777,425	02/12/2004	Paul R. Sanberg	1372.129.PRC	4329

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EXAMINER	
KIM, TAEYOON	
ART UNIT	**PAPER NUMBER**
1651	

NOTIFICATION DATE	DELIVERY MODE
06/29/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)
	10/777,425	SANBERG ET AL.
	Examiner	Art Unit
	TAEYOON KIM	1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-12,14 and 16-26* is/are pending in the application.

4a) Of the above claim(s) *19-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-12,14 and 16-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)	
1) ☒ Notice of References Cited (PTO-892)	4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) ☐ Notice of Informal Patent Application
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.	6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response filed on 4/20/2011 has been received and entered into the case.

Claims 2-4, 13 and 15 have been canceled, claims 19-26 are withdrawn from consideration as being drawn to non-elected subject matter, and claims 1, 5-12, 14 and 16-18 have been considered on the merits. All arguments have been fully considered.

The claim rejection under 35 U.S.C.§112, new matter rejection, has been withdrawn based on the argument presented in the current amendment and 1.132 declaration by Walter Low filed on 4/20/2011.

Claim Objections

Claim 1 is objected to because of the following informalities: The phrase "has not been cultured" in line 5 of claim 1 appears to be more appropriate as "that has not been cultured" or "without culturing in vitro". Appropriate correction is required.

Claim 12 is objected to because of the following informalities: It is more appropriate to add the term "and" between two steps of the obtaining step and the administering step. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 5-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 discloses the phrase "generating myocyte further comprising" in line 6. It is not clear whether the step of generating myocyte is a separate step which comprises the following administering step in addition to the generating step. In other words, it is not clear whether generating myocyte is carried out prior to the administering step or generating myocytes is the consequence of the administering step. Clarification is required.

It appears that applicant claims the latter. If this is the case, it is not necessary to disclose the step of "generating myocyte". It is suggested that the phrase can be replaced with the term "and".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 5-12 and 14-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pittenger et al. (US 6,387,369; of record) in view of Dengler et al. (2002, Herz; of record) in further view of Edelberg et al. (US 2003/0091547; of record), Isner et al. (US 5,980,887; of record), Erices et al. (2000, British J. Haematol.; IDS ref.; of record), Lim et al. (1999, Bone Marrow Transplantation; IDS ref.; of record) and Bruder et al. (US 6,355,239).

Pittenger et al. teach a method of regenerating cardiac muscle using mesenchymal stem cells (MSCs) (see abstract). Pittenger et al. teach human MSCs being introduced to the infarct zone (myocardial infarction; cardiac injury) to reduce the degree of scar formation and to augment ventricular function (treating a circulatory disorder; col. 4, lines 7-19). Pittenger et al. also teach direct or systemic administration (col. 2, lines 25-30) and an amount of cells for administration being 10-40x10^6 MSCs/ml (col. 4, lines 65-67).

Although Pittenger et al. do not teach umbilical cord blood cells used in the method, it would have been obvious to a person of ordinary skill in the art to substitute MSCs of Pittenger with UCBCs. This is because Dengler et al. teach that UCBCs comprise stem cells with a capability of differentiating into cardiac myocytes (p.604, right col. under "umbilical cord stem cells"), Edelberg et al. teach that endothelial progenitor cells, which can also differentiate into cardiomyocytes, are also present in UCB (par. 18 and 24), and Isner et al. teach the use of endothelial progenitor cells derived from UCB in treating of cardiovascular disorder and therefore, a person of ordinary skill in the art would recognize suitability of UCBCs an alternative to MSCs of Pittenger et al. in the method of treating cardiovascular dysfunctions.

M.P.E.P. §2144.07 states "The selection of a known material based on its suitability for its intended use supported a prima facie obviousness determination in Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945) (Claims to a printing ink comprising a solvent having the vapor pressure characteristics of butyl carbitol so that the ink would not dry at room temperature but would dry quickly upon heating were held invalid over a reference teaching a printing ink made with a different solvent that was nonvolatile at room temperature but highly volatile when heated in view of an article which taught the desired boiling point and vapor pressure characteristics of a solvent for printing inks and a catalog teaching the boiling point and vapor pressure characteristics of butyl carbitol. "Reading a list and selecting a known compound to meet known requirements is no more ingenious than selecting the last piece to put in the last opening in a jig-saw puzzle." 325 U.S. at 335, 65 USPQ at 301.)".

With regard to the limitation directed to the UCBC having not been cultured, Pittenger et al. in view of Dengler et al. do not teach the limitation. However, it would have been obvious to a person of ordinary skill in the art to use isolated UCBC cells without culturing (i.e. without expansion). This is because Isner et al. teach that hematopoietic stem/progenitor cells are administered to a patient after separation, which can be stored in cryogenic condition, or optionally the cells may be expanded ex vivo (culturing) (col. 7, lines 8-15). Furthermore, Bruder et al. teach that mesenchymal stem cells can be used without culture expansion (col. 3, lines 10-19). Thus, using isolated stem/progenitor cells without culturing/expansion is a well-known option in stem cell therapy art, and thus, a person of ordinary skill in the art would certainly use the UCBC of Dengler et al. in the method of Pittenger et al. without culturing or expansion prior to

the administration.

Although Dengler et al. do not particularly teach that UCBCs are mesenchymal cells, it is well known in the art that UCBCs comprises mesenchymal progenitor cells according to Erices et al. Therefore, the UCBCs of Dengler et al. inherently comprise mesenchymal cells.

Although Pittenger et al. in view of Dengler et al. and Edelberg et al. do not teach the limitation of administering the UCBCs within approximately 48 hours after the onset of myocardial infarction, a person of ordinary skill in the art would recognize that the range of hours for administration of UCBCs is a result-effective variable. As such, the variables would be routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by those references. Generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); >see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); ** In re Hoeschele, 406 F.2d 1403, 160 USPQ 809

(CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Accordingly, the claimed invention was prima facie obvious to one of ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

With regard to the limitation of the umbilical cord blood composition comprising at least 6 million white blood cells per milliliter, the use of UCBCs in a method of treating myocardial infarction as taught by Pittenger et al. in view of Dengler et al. in further view of Edelberg et al. inherently meets the limitation of the white blood cell contents, since Lim et al. teach that UCB contains about 11 million white blood cells per ml (see Table 1).

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Claims 1, 5-12, 14 and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over DiGiusto et al. (1996, Blood) in view of Dengler et al. (2002, Herz; of record), Erices et al. (2000, British J. Haematol.; of record) and Lim et al. (1999, Bone Marrow Transplantation; of record).

DiGiusto et al. teach a method of administering cryopreserved UCB progenitor cells (LDMNC) without further manipulation after thawing for donor reconstitution (see p.1266, right col.). According to DiGiusto et al., cryopreserved cells have been processed at the site of collection (see p. 1262, under "Materials and Methods"), and thus, the cryopreserved UCB progenitor cells were not cultured in vitro prior to cryopreservation, and since DiGiusto et al. utilized the cryopreserved cells without further manipulation after thawing, it would be interpreted as the UCB cells that have not been cultured or without culturing in vitro, and thus meets the claimed limitation.

Although DiGiusto et al. do not teach a method of treating a circulatory disorder, it would have been obvious to a person of ordinary skill in the art to try UCB cells of DiGiusto et al. in a method of treating cardiomyopathy, myocardial infarction or congenital heart disease.

This is because Dengler et al. teach that UCBCs comprise stem cells with a capability of differentiating into cardiac myocytes (p.604, right col. under “umbilical cord stem cells”), and thus, it would have been obvious to a person of ordinary skill in the art to use UCB cells of DiGiusto et al. for treating cardiomyopathy as taught by Dengler et al. with a reasonable expectation of success.

While DiGiusto et al. is silent that UCB cells contain mesenchymal progenitor/stem cells, however, it is well known in the art that UCB cells contain mesenchymal progenitor cells according to Erices et al. (see entire document), and thus, it is expected that UCB cells of DiGiusto et al. contain mesenchymal progenitor cells.

Although DiGiusto et al. in view of Dengler et al. and Erices et al. do not teach the limitation of administering the UCBCs within approximately 48 hours after the onset

of myocardial infarction, a person of ordinary skill in the art would recognize that the range of hours for administration of UCBCs is a result-effective variable. As such, the variables would be routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by those references. Generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); >see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); ** In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Accordingly, the

claimed invention was prima facie obvious to one of ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

With regard to the limitation of the umbilical cord blood composition comprising at least 6 million white blood cells per milliliter, the use of UCBCs in a method of treating myocardial infarction as taught by DiGiusto et al. in view of Dengler et al. and Erices et al. inherently meets the limitation of the white blood cell contents, since Lim et al. teach that UCB contains about 11 million white blood cells per ml (see Table 1).

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAEYOON KIM whose telephone number is (571)272-9041. The examiner can normally be reached on 8:00 am - 5:00 pm ET (Mon-Thu).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Taeyoon Kim/
Primary Examiner, Art Unit 1651